Internal Medicine
The Japanese Society of Internal Medicine
doi: 10.2169/internalmedicine.0313-17
Intern Med 57: 2057-2060, 2018
http://internmed.jp

【 CASE REPORT 】

The Differential Diagnosis of Acute Onset Truncal Ataxia: The Importance of Dysgeusia in Miller Fisher Syndrome

Tatsuya Ueno, Ryoya Kimura, Tomoya Kon, Rie Haga, Haruo Nishijima, Jin-ichi Nunomura and Masahiko Tomiyama

Abstract:
Miller Fisher syndrome (MFS) can be difficult to diagnose, particularly in mild cases where some of the standard triad of symptoms (external ophthalmoplegia, ataxia, and loss of deep tendon reflex) are absent. We herein report a case of the incomplete form of MFS diagnosed in a 54-year-old Japanese man who presented only with ataxia symptoms and was positive for the anti-GQ1b antibody. However, the patient also suffered from dysgeusia, a significant impairment of taste perception. We propose that dysgeusia in acute-onset ataxia cases may constitute an important clinical feature to aid in the diagnosis of the incomplete form of MFS.

Key words: dysgeusia, taste impairment, ataxia, Miller Fisher syndrome, GQ1b, differential diagnosis

(Intern Med 57: 2057-2060, 2018)
(DOI: 10.2169/internalmedicine.0313-17)

Introduction

Miller Fisher syndrome (MFS) is typically characterized by a triad of clinical symptoms [external ophthalmoplegia, ataxia, and loss of deep tendon reflex (DTR)] (1) and the presence of immunoglobulin G (IgG) antibodies against GQ 1b gangliosides (2). The incomplete form of MFS, however, is characterized by acute ophthalmoparesis, acute ataxic neuropathy (AAN), acute ptosis, and acute mydriasis (2). Anti-GQ1b antibodies are also found in Bickerstaff brainstem encephalitis and in acute ophthalmoplegia without ataxia, which are collectively referred to as "anti-GQ1b antibody syndrome" (3). A growing body of evidence suggests that dysgeusia may represent an additional neurological symptom of MFS (1, 4-9). However, whether or not dysgeusia is also observed in cases of the incomplete form of MFS that present without all three triad symptoms is unclear.

We herein report a rare case of truncal ataxia with dysgeusia, due to AAN, that did not present with the other two triad symptoms. The present case suggests that dysgeusia may be useful for the differential diagnosis of MFS from other ataxia-related diseases. The patient provided his written informed consent for the publication of this report.

Case Report

A 54-year-old Japanese man was admitted to our department for the evaluation of gait disturbance, dysgeusia, and dysarthria, in addition to numbness in all four limbs and in the perioral area. Twelve days before the admission, he had nasal discharge and sore throat symptoms, indicating an upper respiratory infection. The patient also experienced gait unsteadiness seven days prior to admission and dysarthria accompanied by numbness in all four limbs and in the perioral area six days before admission. Furthermore, he could not perceive the salty taste of miso soup five days prior to admission. His medical history included postoperative mitral regurgitation and the insertion of a prosthetic right eye following a car accident. He did not drink alcohol and had no history of suspected toxic exposure to metals or solvents.

On admission, his vital signs were unremarkable. His Glasgow coma scale score was 15 (E4V5M6). A physical examination showed no lesions of the oral mucosa. A neurological examination revealed a wide-based gait, a tandem stance impairment, slightly slurred speech, and hypesthesia for cold sensation in his distal limbs. The left pupil was 3 mm in diameter with a prompt reactivity to light. The left extraocular movement was normal. There were no indica-

Department of Neurology, Aomori Prefectural Central Hospital, Japan
Received: October 4, 2017; Accepted: December 5, 2017; Advance Publication by J-STAGE: February 28, 2018
Correspondence to Dr. Tatsuya Ueno, lacote19thg@gmail.com and tatsuya_ueno@med.pref.aomori.jp

tions of facial nerve palsy. Both the DTR and deep sense of the limbs were normal, as was the jaw reflex. The bilateral plantar responses were flexor. There were no signs of limb weakness or limb ataxia. Although he could taste sweet and bitter foods normally, he found that oranges tasted bitter. Furthermore, he complained of a reduced ability to taste salty foods.

Laboratory evaluations showed normal levels of vitamin B_1 (37 ng/mL), vitamin B_{12} (537 pg/mL), folate (7.2 ng/mL), total homocysteine (9.5 nmol/mL), blood glucose (107 mg/dL), hemoglobin A1c (5.7%), and Zn (90.0 μg/dL). Anti-SS-A/Ro and anti-SS-B/La antibody tests were all negative. A pharyngeal culture revealed *Haemophilus species*. A cerebrospinal fluid (CSF) analysis revealed normal cell counts (3 cells/μL), a total protein level of 24 mg/dL, and a glucose level of 62 mg/dL, with a concomitant blood glucose level of 107 mg/dL and a normal IgG index (0.63). Oligoclonal bands were negative. The Schirmer test, the Rose Bengal test, and gum test were all negative. Motor and sensory nerve conduction evaluations showed no abnormalities, including the minimal F-wave latency. Brain magnetic resonance imaging (MRI) findings was normal. Based on these results, we hypothesized that acute onset ataxia and peripheral neuropathy, resulting from AAN, were the likely causes of the clinical portrait of the patient.

After admission, we carefully monitored the patients' neurological symptoms; however, no immunotherapy was prescribed due to his mild symptoms. On day three after admission, the dysarthria and the taste impairment disappeared. On day seven, both the truncal ataxia and the limb and perioral numbness were found to have improved. He was discharged on day 14 after admission. The patient was never treated with immunotherapy because follow-up assessments revealed that the ataxia never deteriorated, that there was no loss of DTR, and that eye movements were not restricted. On day 39 after the onset, enzyme-linked immunosorbent assays taken from a specimen at admission showed no IgG or IgM antibodies reacting with gangliosides GM1, GM2, GM3, GD1a, GD1b, GD3, GT1b, galactocerebroside, GalNAc-GD1a, or GD1a/GD1b. However, IgG reacting with GQ1b and GT1a were positive. We therefore finally diagnosed the patient with AAN.

Discussion

This case suggests that dysgeusia in acute-onset ataxia may constitute an important clinical feature to assist in the diagnosis of the AAN presenting without DTR abnormalities or external ophthalmoplegia. Midline cerebellar lesions are known to cause truncal ataxia (10). The differential diagnosis of sporadic ataxia cases that include truncal ataxia can be complicated, given the wide variety of diseases and conditions that present with similar symptoms: chronic alcohol use, exposure to toxic agents, immune-mediated inflammation (paraneoplastic cerebellar degeneration, anti-glutamic acid decarboxylase antibodies ataxia, Hashimoto encephalopathy), vitamin deficiency (a deficiency in vitamin B_1, vitamin B_{12}, or vitamin E), chronic infections, neurodegenerative diseases, hereditary spinocerebellar ataxias, brain tumors, strokes, vestibular neuritis, Sjögren syndrome, and MFS (6, 10-16). Our patient presented with dysgeusia, limb and perioral numbness, and acute-onset truncal ataxia. Although our patient had no limb weakness and presented with normal DTR and nerve conduction, the symmetric limb and perioral numbness combined with the presence of dysgeusia suggested a potential diagnosis of peripheral neuropathy. Similarly, Sjögren syndrome is characterized by a sensory ataxic neuropathy due to an impairment of the joint-position sense and dysgeusia (15, 17). In Sjögren syndrome, however, paraesthesia is mostly asymmetrical, segmental, or multi-focal, rather than presenting as a symmetrical polyneuropathy, and usually develops over several months to several years (15). Furthermore, mouth dryness is usually present for years prior to the onset of dysgeusia in Sjögren syndrome (17). Given the uncharacteristic time course of the symptom evolution in our patient, we ruled out Sjögren syndrome as a possible diagnosis. We initially considered AAN as a diagnosis based on our patient's history of acute onset, upper respiratory infection, and pattern of neurological findings, and we made the final diagnosis following the confirmation of positivity for anti-GQ1b antibody. Although the evidence supporting a central cause of ataxia in MFS is weak at present (18), our patient exhibited slightly slurred speech in the absence of facial nerve palsy and bulbar palsy. Therefore, central causes may also be considered in this case.

The present findings, combined with those of the previous reports regarding the presence of dysgeusia in MFS patients (Table) (1, 4-9), suggest that dysgeusia may constitute a rare clinical symptom of MFS. Dysgeusia occurs in approximately 0.6-2% patients with Guillain-Barré syndrome (GBS) (19, 20), although we previously found that dysgeusia was present in 6 out of 10 consecutive GBS patients (21). Furthermore, 20% of these patients spontaneously complained of taste impairments, and detailed medical history charts revealed that 40% of patients had a taste impairment (21). Although our patient had truncal ataxia without absent/decreased DTR or extraocular movement abnormalities, we were able to recognize dysgeusia early on because he spontaneously reported a taste impairment. The previous seven cases of MFS presenting with dysgeusia had typical MFS neurological features, including external ophthalmoplegia, ataxia, and an absence of DTR (1, 4-9), and were all treated with intravenous gamma globulin, with the exception of one case (1). In contrast, although we were unable to evaluate the presence of double vision and the extraocular movement of the right eye because our patient had previously lost an eye, this case presented with truncal ataxia and symmetric limb and perioral numbness, both of which spontaneously improved without immunotherapy. We therefore believe that course of the present case was consistent with AAN. Consequently, dysgeusia may constitute an

Table. **Clinical Features of Patients with Dysgeusia Due to Miller-Fisher Syndrome.**

Reference	Age	Sex	EO	Ataxia	DTR	Dysgeusia	FNP	Antecedent infection	Treatment	Dysgeusia recovery period
1	49	M	Complete EO	Limb and truncal ataxia	Absent	Yes, but no report of modality	Delayed onset	URI	No	NR
5	38	M	Diplopia at left gaze	Limb and truncal ataxia	Absent	Salty taste, sour taste and bitter taste	None	URI	IVIg	5 days
4	41	M	Incomplete EO	Truncal ataxia	Absent	Strange taste	None	Gastroenteritis	IVIg	NR
6	60	F	Complete EO	Truncal ataxia	Absent	Sweet taste and salty taste	None	URI	IVIg	Sweet taste, 7 days; Salty taste, 12 days
7	53	M	Impairment of abduction, adduction and supraduction	Limb and truncal ataxia	Absent	Yes, but no report of modality	None	URI	IVIg	35 days
9	50	M	Severe abduction palsy	Limb and truncal ataxia	Absent	Yes, but no report of modality	None	URI	IVIg	NR
8	55	M	Complete EO	Limb and truncal ataxia	Absent	All taste	Delayed onset	URI	IVIg	42 days
Present case	54	M	Normal	Truncal ataxia	Normal	Salty taste, and strange taste	None	URI	No	9 days

F: female, M: male, EO: external ophthalmoplegia, DTR: deep tendon reflex, FNP: facial nerve palsy, URI: upper respiratory infection, IVIg: intravenous immunoglobulin, NR: not reported

important clinical feature to aid in the diagnosis of MFS, even when the diagnosis is challenging, such as in cases of AAN.

Dysgeusia in GBS is believed to result from a lesion of the chorda tympani branch of the facial nerve or from the involvement of an accessory taste pathway through the trigeminal nerve (20). In MFS, Uchibori et al. speculated that anti-GQ1b antibodies may affect the peripheral nerves associated with taste and taste buds (5). In the present case, dysgeusia improved quickly, likely because the taste receptors turnover in as little as 10 days (6). Alternatively, an accessory taste pathway through the trigeminal nerve may also be involved in dysgeusia, as our patient showed perioral numbness without facial nerve palsy.

In conclusion, dysgeusia in acute-onset ataxia may constitute an important clinical feature to aid in the diagnosis of AAN, an incomplete form of MFS. Physicians should investigate potential complaints of dysgeusia in patients with acute-onset ataxia.

The authors state that they have no Conflict of Interest (COI).

Acknowledgement

The authors would like to thank Susumu Kusunoki, Professor of the Department of Neurology, Kindai University Faculty of Medicine, Osaka, Japan, for the anti-ganglioside antibody analysis.

References

1. Fisher M. An unusual variant of acute idiopathic polyneuritis (syndrome of ophthalmoplegia, ataxia and areflexia). N Engl J Med **255**: 57-65, 1956.

2. Wakerley BR, Uncini A, Yuki N; GBS Classification Group. Guillain-Barré and Miller Fisher syndromes--new diagnostic classification. Nat Rev Neurol **10**: 537-544, 2014.

3. Odaka M, Yuki N, Hirata K. Anti-GQ1b IgG antibody syndrome: clinical and immunological range. J Neurol Neurosurg Psychiatry **70**: 50-55, 2001.

4. Dörr J, Dieste FJ, Klaasen van Husen D, Zipp F, Vogel HP. A case of recurrent Miller Fisher syndrome mimicking botulism. Neurol Sci **27**: 424-425, 2006.

5. Uchibori A, Kashiwagi T, Takeuchi S, Chiba A, Sakuta M. Case of Fisher syndrome with impairment of taste. Rinsho Shinkeigaku (Clin Neurol) **46**: 281-284, 2006 (in Japanese, Abstract in English).

6. Ohe Y, Shintani D, Kato Y, Tanahashi N. Fisher syndrome with taste impairment. Intern Med **51**: 2977-2979, 2012.

7. Yagi Y, Yokote H, Watanabe Y, Amino T, Kamata T, Kusunoki S. Taste impairment in Miller Fisher syndrome. Neurol Sci **36**: 809-810, 2015.

8. Yamamoto D, Suzuki S, Hirose B, Yamada M, Shimizu M, Shimohama S. Fisher syndrome with delayed facial weakness and taste impairment: a case report. Rinsho Shinkeigaku (Clin Neurol) **56**: 684-689, 2016 (in Japanese, Abstract in English).

9. Yepishin IV, Allison RZ, Kaminskas DA, Zagorski NM, Liow KK. Miller Fisher syndrome: a case report highlighting heterogeneity of clinical features and focused differential diagnosis. Hawaii J Med Public Health **75**: 196-199, 2016.

10. Daroff RB, Jankovic J, Mazziotta JC, Pomeroy SL. Bradley's Neurology in Clinical Practice. 7th ed. Elsevier, Philadelphia, 2015.

11. Ogawa K, Suzuki Y, Oishi M, Kamei S. Clinical study of 46 patients with lateral medullary infarction. J Stroke Cerebrovasc Dis **24**: 1065-1074, 2015.
12. Carmona S, Martinez C, Zalazar G, et al. The diagnostic accuracy of truncal ataxia and HINTS as cardinal signs for acute vestibular syndrome. Front Neurol **7**: 125, 2016.
13. Ogawa K, Suzuki Y, Takahashi K, Akimoto T, Kamei S, Soma M. Clinical study of seven patients with infarction in territories of the anterior inferior cerebellar artery. J Stroke Cerebrovasc Dis **26**: 574-581, 2017.
14. Zaro-Weber O, Galldiks N, Dohmen C, Fink GR, Nowak DA. Ocular flutter, generalized myoclonus, and trunk ataxia associated with anti-GQ1b antibodies. Arch Neurol **65**: 659-661, 2008.
15. Mori K, Iijima M, Koike H, et al. The wide spectrum of clinical manifestations in Sjögren's syndrome-associated neuropathy. Brain **128**: 2518-2534, 2005.
16. Klockgether T. Sporadic ataxia with adult onset: classification and diagnostic criteria. Lancet Neurol **9**: 94-104, 2010.
17. Berkowitz AL, Samuels MA. The neurology of Sjögren's syndrome and the rheumatology of peripheral neuropathy and myelitis. Pract Neurol **14**: 14-22, 2014.
18. Shahrizaila N, Yuki N. Bickerstaff brainstem encephalitis and Fisher syndrome: anti-GQ1b antibody syndrome. J Neurol Neurosurg Psychiatry **84**: 576-583, 2013.
19. Winer JB, Hughes RA, Osmond C. A prospective study of acute idiopathic neuropathy. I. Clinical features and their prognostic value. J Neurol Neurosurg Psychiatry **51**: 605-612, 1988.
20. Odaka M, Yuki N, Nishimoto Y, Hirata K. Guillain-Barré syndrome presenting with loss of taste. Neurology **58**: 1437-1438, 2002.
21. Nishijima H, Tomiyama M, Suzuki C, et al. Taste impairment in Guillain-Barre syndrome: more frequent than thought? J Peripher Nerv Syst **16**: 270-271, 2011.